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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/735,995	12/14/2000	Mark Keating	2323-156	6821

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EXAMINER
QIAN, CELINE X

ART UNIT	PAPER NUMBER
1636	8

DATE MAILED: 01/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/735,995	Applicant(s) KEATING ET AL.	
	Examiner Celine X Qian	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 November 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 22-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 22-25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 22-25 are pending in the application.

This Office Action is in response to the Amendment filed on 11/15/02. Claims 11-18, 29 and 30 are cancelled according to the amendment.

Response to Amendment

The rejection of claims 22-25 under 35 U.S.C. 103 (a) has been withdrawn in light of the correction of the priority date of the claims.

The rejection of claims 22-25 under 35 U.S.C 112 first paragraph is maintained for reasons set forth of the record mailed on 6/17/02 and further discussed below.

The rejection of claims 22-25 under 35 U.S.C 112 second paragraph is maintained for reasons set forth of the record mailed on 6/17/02 and further discussed below.

Response to Arguments

35 USC § 112, first paragraph

Claims 22-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method to screen for drugs which are useful in treating a person of LQT syndrome resulting from a mutation in HERG, wherein said mutation is one which results in a cysteine at amino acid 572, an aspartic acid at 588, a valine at 614, an alanine at 630 or a lysine at 29, by measuring K+ channel conductance in cells expressing wild type or mutant HERG, does not reasonably provide enablement for said method to screen for drugs which are useful in treating any disease with a mutation in HERG. In addition, the method is not enabled when the cells expressing wild type or mutant HERG are obtained from transgenic animal. The

specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

In response to the 112 first paragraph rejection, Applicants argue that all five mutations claimed in the HERG gene are in critical regions of the HERG and affect K+ ion channel activation. Applicants further cite references that teach these mutations are linked to LQT syndrome. Applicants assert that claim 25 does not require that the transgenic animal be of a specific phenotype, but only the cells are derived from a transgenic animal. Applicants further argue that the Examiner fails to explain why these cells derived from transgenic animal cannot be altered by transformation to express a wild type or mutant HERG.

These arguments have been considered and deemed partially persuasive. The instant specification while being enabling for a method to screen for drugs which are useful in treating a person of LQT syndrome resulted from a mutation in HERG, wherein said mutation is one which results in a cysteine at amino acid 572, an aspartic acid at 588, a valine at 614, an alanine at 630 or a lysine at 29, by measuring K+ channel conductance in cells expressing wild type or mutant HERG, does not support for the enablement of such method to screen for drugs which are useful in treating any disease associated with one of the specified mutations in HERG. Further, the specification does not enable such a method wherein the cells expressing wild type or mutant HERG are obtained from transgenic animal.

The state of the art at the time of filing only links HERG mutations to LQT syndrome. The mutations disclosed by the specification are identified from genomic samples of LQT kindred. As such, although HERG mutations result a change in K+ channel conductance that has been identified in LQT patients, such mutation is not link to any other known disease.

Therefore, a method for identifying drugs for treating a person with a mutation in HERG by comparing K+ conductance of the cells expressing wild type and the mutant HERG is unpredictable. The method is only enabled for identifying drugs to treat LQT.

As discussed in the previous office action, claim 25 is enabled only if the transgenic animal comprising mutant HERG gene in its genome and exhibit altered K+ channel current in all cells of said animal. However, it is unclear whether the specific mutations disclosed in the specification would cause altered K+ channel current in the transgenic mouse because the mouse already have the wild type HERG in its genome. In addition, the disclosed mutation is in human sequence, and whether mutation in the same site in mouse gene would result in alteration of K+ channel is unpredictable because the human HERG and mouse HERG are not identical. There is no teaching in the specification regarding the phenotype of the cells isolated from the transgenic mouse having its own wild type HERG further comprising a human wild type HERG or mutants with disclosed mutations. Therefore, claim 25 is not enabled as claimed. Applicants argue that the cells derived from the transgenic animal can be transformed with wild type or mutant HERG. However, the claim does not recite this transformation step. In addition, the specification does not teach such a method wherein the cells derived from any transgenic animal are transformed with a wild type or mutant HERG. Therefore, one skilled in the art would have to engage in undue experimentation to practice the method as claimed.

New Grounds of Rejection Necessitated by the Amendment

35 USC § 112, second paragraph

Claims 22-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 22-25, the term "bathing solution" renders the claims indefinite because it is unclear how a "bathing" solution can be suitable for measuring K+ conductance. It appears that Applicants are referring to specific solution for measuring K+ conductance.

Clarification is needed.

Claim 23 recites the limitation "a leucine at amino acid residue 29" in line 4. There is insufficient antecedent basis for this limitation in the claim. The parent claim (22) recites "a lysine" rather than "a leucine" at amino acid residue 29.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Celine Qian, Ph.D.
January 27, 2003

Anne-Marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER